

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1-109. (canceled)

110. (currently amended) A ~~thermodynamic~~ method for ~~predicting duplex stability of~~ designing an oligonucleotide sequence having a selected duplex stability comprising at least one modified nucleotide base, said method comprising:

a) providing an oligonucleotide having a sequence of N bases and N-1 neighboring base pairs, wherein said oligonucleotide comprises at least one modified base selected from the group consisting of a universal base, unsubstituted and 3-substituted pyrazolo[3,4-d]pyrimidines and unsubstituted and 5-substituted pyrimidines; and

b) calculating the duplex stability of said oligonucleotide using an algorithm applying a nearest-neighbor model for duplex formation thermodynamics for each of the N-1 neighboring base pairs, each nearest neighbor thermodynamic parameter defining a thermodynamic contribution of two corresponding neighboring bases, optionally repeating steps a)-b) to obtain a sequence having said selected duplex stability.

111. (currently amended) A method for ~~predicting the melting temperature (T_m) of~~ designing an oligonucleotide sequence having a selected duplex stability comprising at least one modified nucleotide base, said method comprising:

a) providing an oligonucleotide having a sequence of N bases and N-1 neighboring base pairs, wherein said oligonucleotide comprises at least one modified base selected from the group consisting of a universal base, unsubstituted and 3-substituted pyrazolo[3,4-d]pyrimidines and unsubstituted and 5-substituted pyrimidines; and a minor groove binder; and

b) calculating a melting temperature (T_m) of said oligonucleotide using an algorithm applying nearest neighbor thermodynamic parameters for each of the N-1 neighboring base pairs, each nearest neighbor thermodynamic parameter defining a thermodynamic contribution of two corresponding neighboring bases, optionally repeating steps a)-b) to obtain a sequence having said selected duplex stability.

112. (previously presented) The method of any one of claims 110 or 111, wherein said oligonucleotide sequence is derived from a database source.

113. (currently amended) The method of claim 112, wherein said ~~oligonucleotide sequence~~ database source is GENBANK ~~derived from Genbank.~~

114. (previously presented) The method of any one of claims 110 or 111, wherein said at least one modified base is a member selected from the group consisting of a base attached to an amino acid, a polyamide nucleic acid (PNA) and a locked nucleic acid sugar.

115. (previously presented) The method of claim 114, wherein said modified base is attached to PNA.

116. (currently amended) The method of claim 114, wherein said modified base is a locked nucleic acid sugar.

117. (currently amended) The method of any one of claims 110 or 111, wherein said oligonucleotide ~~comprising at least one modified base has superior~~ an enhanced ability of mismatch discrimination, in comparison to unmodified nucleotides.

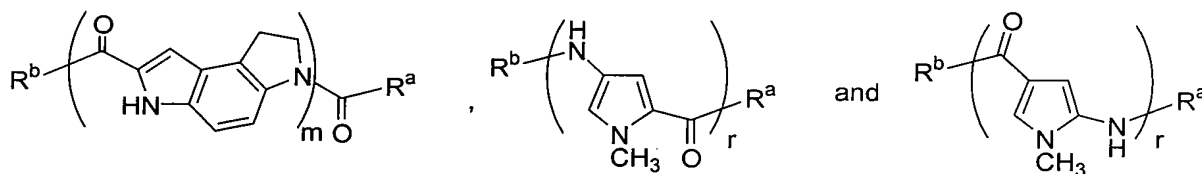
118. (previously presented) The method of any one of claims 110 or 111, wherein said at least one modified base is a member selected from the group consisting of a

universal base, PPA, PPG, PPPA, PPPG, PU, PC, HOPU, HOBuU, HOBuC, (NH₂)₂PPPA, (NH₂)₂PPPAOH, (NH₂)₂BuPPAOH, (NH₂)₂PPAI, and HOBuPPG.

119. (currently amended) The method of claim ~~any one of claims 110 or 111~~, wherein said oligonucleotide has attached to it one or more members selected from the group consisting of a minor groove binder, a fluorophore and a quencher.

120. (previously presented) The method of claim **119**, wherein said oligonucleotide sequence has a minor groove binder attached thereto.

121. (currently amended) The method of claim 111 or **120**, wherein said minor groove binder has a formula selected from the group consisting of:



wherein

the subscript m is an integer of from 2 to 5;

the subscript r is an integer of from 2 to 10; and

each R^a and R^b is independently a linking group to said modified oligonucleotide, H, OR^c, NR^cR^d, COOR^c and -CONR^cR^d wherein each R^c and R^d is selected from the group consisting of H, (C₁-C₁₂)heteroalkyl, (C₂-C₁₂)heteroalkenyl, (C₂-C₁₂)heteroalkynyl, (C₁-C₁₂)alkyl, (C₂-C₁₂)alkenyl, (C₂-C₁₂)alkynyl, aryl(C₁-C₁₂)alkyl and aryl.

122. (previously presented) The method of claim **120**, wherein said minor groove binder is attached to the oligonucleotide via a quencher molecule.

123. (previously presented) The method of any one of claims **110** or **111**, wherein said algorithm predicts the melting temperature (T_m) of said oligonucleotide with an accuracy of about $\pm 2^\circ\text{C}$.

124. (currently amended) The method of any one of claims **110** or **111**, wherein said method is applied to establish ~~in establishing appropriate~~ conditions for hybridization, renaturation, mapping variations of base compositions of sequences or determination of sequence complexity and divergence.

125. (previously presented) The method of any one of claims **110** or **111**, wherein said oligonucleotide is a capture probe in an array.

126. (currently amended) The method of claim **115**, wherein said oligonucleotide ~~comprising at least one modified base~~ has superior an enhanced ability of mismatch discrimination, in comparison to unmodified nucleotides.

127. (currently amended) The method of claim **116**, wherein said oligonucleotide ~~comprising at least one modified base~~ has superior an enhanced ability of mismatch discrimination, in comparison to unmodified nucleotides.